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S/N 09/645,706

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Keith V. Wood et al.

Examiner: Rebecca Prouty

Serial No.: 09/645,706

Group Art Unit: 1652

Filed: August 24, 2000

Docket: 341.005US1

Title: SYNTHETIC NUCLEIC ACID MOLECULE COMPOSITIONS AND
METHODS OF PREPARATION

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12/4/02

RESPONSE TO RESTRICTION REQUIREMENT

Commissioner for Patents
Washington, D.C. 20231

In response to the Restriction Requirement mailed September 10, 2002, Applicant provisionally elects, with traverse, the claims of Group I (claims 1-45, 47, 54, and 60-64), directed to a synthetic nucleic acid molecule comprising at least 300 nucleotides of a coding region for a polypeptide, having a codon composition differing at more than 25% of the codons from a wild type nucleic acid sequence encoding a polypeptide, and having at least 3-fold fewer transcription regulatory sequences relative to the average number of such sequences resulting from random selections of codons at the codons which differ, wherein the transcription regulatory sequences are selected from the group consisting of transcription factor binding sequences, intron splice sites, poly(A) addition sites and promoter sequences, and wherein the polypeptide encoded by the synthetic nucleic acid molecule has at least 85% sequence identity to the polypeptide encoded by the wild type nucleic acid sequence; a plasmid or expression vector comprising the synthetic nucleic acid molecule; a host cell or kit comprising the expression vector; a polynucleotide which hybridizes under stringent hybridization conditions to SEQ ID NO:22 (Rluc-final), SEQ ID NO:9 (GRver5.1), SEQ ID NO:18 (RD156-1H9), SEQ ID NO:297 (GRver5.1), SEQ ID NO:301 (RD156-1H9), or the complement thereof; a synthetic molecule prepared by a method which comprises altering a plurality of transcription regulatory sequences, and altering greater than 25% of codons, in a nucleic acid sequence which encodes a polypeptide having at least 100 amino acids; and a vector comprising a synthetic nucleic acid molecule having at least 3-fold fewer transcriptional regulatory sequences relative to a vector comprising a parent nucleic acid sequence, wherein the transcription regulatory sequences are selected from

the group consisting of transcription factor binding sequences, intron splice sites, poly(A) addition sites and promoter sequences.

With respect to the requirement to elect a species from sequences recited in claims 17-19, Applicant provisionally elects, with traverse, the species SEQ ID NO:9. Claims 1-7, 9, 11-12, 15, 18, 20-21, 24-33, 35-39, 41-45, 54, 60-61, and 63 read on SEQ ID NO:9.

Reconsideration and withdrawal of the Restriction Requirement and election of species, in view of the remarks herein, is respectfully requested.

Applicant's invention includes synthetic nucleic acid molecules possessing one or more desirable properties, methods to prepare synthetic nucleic acid molecules possessing one or more desirable properties, and polypeptides encoded by the synthetic nucleic acid molecules. The methods generally include altering a plurality of transcription regulatory sequences and altering greater than 25% of codons in a parent nucleic acid sequence which encodes a polypeptide having at least 100 amino acids. The alterations in a parent nucleic acid sequence result in a synthetic nucleic acid sequence which, when introduced to a selected host cell, is expressed more efficiently than the parent nucleic acid sequence. For instance, a nucleic acid sequence that encodes a beetle luciferase and another that encodes a *Renilla* luciferase were altered to yield humanized sequences encoding a luciferase, e.g., sequences encoding a beetle luciferase which emits green light such as SEQ ID NO:7 (GRver5), SEQ ID NO:8 (GRver6), SEQ ID NO:9 (GRver5.1), and SEQ ID NO:297 (GRver5.1), sequences encoding a beetle luciferase which emits red light such as SEQ ID NO:14 (RDver5), SEQ ID NO:15 (RDver7), SEQ ID NO:16 (RDver5.1), SEQ ID NO:299 (RDver5.1), SEQ ID NO:17 (RDver5.2), SEQ ID NO:18 (RD156-1H9) and SEQ ID NO:301 (RD156-1H9), and a sequence encoding a *Renilla* luciferase, for example, SEQ ID NO:226.

Thus, the Restriction Requirement is traversed on the basis that the inventions are so closely related within the context of the disclosure of the application that they cannot properly be considered independent and distinct within the statutory meaning of 35 U.S.C. § 121. For instance, claims directed to a synthetic nucleic acid molecule comprising at least 300 nucleotides of a coding region for a polypeptide, having a codon composition differing at more than 25% of the codons from a wild type nucleic acid sequence encoding a polypeptide, and having at least 3-fold fewer transcription regulatory sequences relative to the average number of such sequences

resulting from random selections of codons at the codons which differ, wherein the transcription regulatory sequences are selected from the group consisting of transcription factor binding sequences, intron splice sites, poly(A) addition sites and promoter sequences, and wherein the polypeptide encoded by the synthetic nucleic acid molecule has at least 85% sequence identity to the polypeptide encoded by the wild type nucleic acid sequence; a plasmid or an expression vector comprising the synthetic nucleic acid molecule; a host cell or kit comprising the expression vector; a polynucleotide which hybridizes under stringent hybridization conditions to SEQ ID NO:22 (Rluc-final), SEQ ID NO:9 (GRver5.1), SEQ ID NO:18 (RD156-1H9), SEQ ID NO:297 (GRver5.1), SEQ ID NO:301 (RD156-1H9), or the complement thereof; a synthetic molecule prepared by a method which comprises altering a plurality of transcription regulatory sequences, and altering greater than 25% of codons, in a nucleic acid sequence which encodes a polypeptide having at least 100 amino acids; and a vector comprising a synthetic nucleic acid molecule having at least 3-fold fewer transcriptional regulatory sequences relative to a vector comprising a parent nucleic acid sequence, wherein the transcription regulatory sequences are selected from the group consisting of transcription factor binding sequences, intron splice sites, poly(A) addition sites and promoter sequences (claims 1-45, 47, 54, and 60-64; Group I) are clearly related to a claim directed to an isolated polypeptide encoded by SEQ ID NO:9 (GRver5.1) or SEQ ID NO:18 (RD156-1H9) (claim 46; Group II) and claims directed to methods comprising altering a plurality of transcription regulatory sequences, and altering greater than 25% of codons, in a nucleic acid sequence which encodes a polypeptide having at least 100 amino acids and a method for preparing at least two synthetic nucleic acid molecules which are codon distinct versions of a parent nucleic acid sequence which encodes a polypeptide (claims 48-53, 55-59 and 65-66; Group III).

The Restriction Requirement is also traversed on the basis that Restriction Requirements are optional in all cases. M.P.E.P. § 803. If the search and examination of an entire application can be made without serious burden, the Examiner must examine it on the merits, even though it arguably may include claims to distinct or independent inventions. M.P.E.P. § 803. Moreover, it is submitted that Applicant should not be required to incur the additional costs associated with the filing of multiple divisional applications in order to obtain protection for the claimed subject matter. Due to the relatedness of the subject matter of the claims in Groups I-III as discussed

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above, the claims in Groups I-III can be efficiently and effectively searched in a single search with no additional burden placed on the Examiner. Evidence that the claims in Groups I-III can be efficiently and effectively searched in a single search with no additional burden placed on the Examiner is provided in the Restriction Requirement as the claims are all in the same class (class 435) for search purposes.

In the event the Examiner remains of the opinion that the restriction is proper as stated in the Restriction Requirement, Applicant's Representatives respectfully request rejoinder of at least the claims in Group III with the claims in Group I upon a notice of allowable subject matter for the claims in Group I. M.P.E.P. 821.04.

Thus, the Restriction Requirement is properly traversed. Accordingly, reconsideration and withdrawal of the Restriction Requirement is respectfully requested.

With respect to the requirement to elect a species, the requirement is traversed on the basis that the species have a disclosed relationship. As discussed above, the species in claims 17-19 are humanized luciferase sequences. Accordingly, the requirement for an election of species is properly traversed and reconsideration is respectfully requested. M.P.E.P. 806.04(b).

The Examiner is invited to contact Applicant's Representative if there are any questions regarding this Response or if prosecution of this application may be assisted thereby.

If necessary, please charge any additional fees or credit overpayment to Deposit Account No. 19-0743.

Respectfully submitted,
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CERTIFICATE UNDER 37 CFR 1.8: The undersigned hereby certifies that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail, in an envelope addressed to: Commissioner for Patents, Washington, D.C. 20231, on this 12th day of November, 2002.

Name: Anne M. Richards

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